REMARKS

Applicants acknowledge the rejection of Claims 1, 2 and 4 - 13 over the hypothetical combination of Trinh with Chen and Claims 1, 2 and 4 - 26 over the hypothetical combination of Trinh with Ramtoola. The Applicants have accordingly amended main Claim 1 to clarify the differences of the invention over the prior art. Claim 1 now recites that the nanoparticles have an active ingredient largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles. Support may be found at page 13, lines 5 - 5, page 26, lines 25 - 26, and elsewhere.

Chen discloses a controlled release preparation comprising a polymer matrix loaded with an active compound. The active compound is complexed with a complexing agent such as a metal ion to modify the release of the active compound from the polymer matrix. The Applicants agree that the complexing agent is preferably a metal ion and can include other agents that can form a complex with the active compound. The Applicants also agree that Trinh discloses cyclodextrin complexes as a complexing agent.

However, hypothetically combining Trinh with Chen does not teach or suggest nanoparticles as claimed herein. In accordance with Claim 1 as now clarified, the nanoparticles in the invention have an active ingredient largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles.

This is sharply different from any structure resulting from the substitution of the cyclodextrin taught by Trinh for the metal ion complexing agent of Chen. In other words, hypothetically combining the cyclodextrin complexes of Trinh for the metal ion complexing agents of Chen would still result in the formation of DOX-cyclodextrin complexes and DOX-cyclodextrin polymer complexes as a control release mechanism to provide a system with optimum release of native DOX. This is gleaned from Column 4 beginning at line 3, wherein the Chen mechanism is taught.

As a consequence, there would be a slow release of DOX from the DOX-cyclodextrin complexes and the DOX-cyclodextrin polymer complexes. However, that is not what is claimed herein, wherein the nanoparticles have an active ingredient largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles. In other words, the hypothetical combination would result in release of the active ingredient corresponding to the release of DOX-cyclodextrin complexes, while in the invention the release of DOX and the release of cyclodextrin are different.

Hence, it can be seen that, even in view of a hypothetical substitution of the cyclodextrin complexes of Trinh for the metal ion complexing agent of Chen, the resulting particles would still be sharply different from those as recited in independent Claim 1. The Applicants accordingly respectfully submit that, in view of these structural differences in the resulting products, the hypothetical combination of Trinh with Chen cannot support a rejection of Claims 1, 2 and 4 - 13 under 35 U.S.C. §103. Withdrawal of the rejection as it applies to Trinh and Chen is accordingly respectfully requested.

The hypothetical combination of Trinh with Ramtoola is less relevant than the hypothetical combination of Trinh with Chen. In that regard, Ramtoola discloses complexing insulin with polycyanoacrylate to form polyalkylcyanoacrylate complexed insulin loaded nanoparticles. However, no mention is made of a complexing agent of any type. The disclosure of Ramtoola makes it clear that the complexing between the polyakylcyanoacrylate and the insulin is completely sufficient for the purposes of Ramtoola. Therefore, there simply would be no motivation of one of ordinary skill in the art to look to Trinh for a complexing agent. At least in the case of Chen, Chen suggests a complexing agent and that other possible complexing agents could be used beyond those specifically taught. Ramtoola has no such teaching and no such suggestions with respect to looking elsewhere for complexing agents. Thus, the motivation for the hypothetical combination is absent between Trinh and Ramtoola.

In any event, even if one of ordinary skill in the art were to make the hypothetical combination, irrespective of the lack of teachings to do so, there is utterly no suggestion in either of Trinh or Ramtoola that resulting nanoparticles would have a polymeric nucleus containing an active ingredient largely contained in the nanoparticle matrix network and the cyclic oligosaccharide molecules are localized on the surface of the nanoparticles. There is simply nothing in either disclosure that even remotely discloses, teaches or suggests this claimed aspect of the invention. The Applicants therefore respectfully submit that the hypothetical combination of Trinh with Ramtoola cannot support a rejection of Claims 1, 2 and 4 - 26. Withdrawal of the rejection is accordingly respectfully requested.

The invention provides numerous advantages in several forms. For example, the invention can provide a nanoparticle with a polymeric nucleus containing a portion of the active ingredient in a molecular state and a surface containing another portion of the active ingredient in a complexed state with the cyclic oligosaccharide which is what is observed with progesterone (or other steroids) and saquinavir.

The cyclic oligosaccharide such as cyclodextrin has both a solubilizing effect on the active ingredient and a stabilizing effect on the active ingredient.

When the active ingredient is hydrophobic, amphiphilic or insoluble such as in the case of hormones, the cyclic oligosaccharide has an important effect on its solubilization which explains the presence of a portion of the active ingredient in a complexed state with the cyclic oligosaccharide.

The active ingredient is a bi-phase release. The rapid release is due to the portion of active ingredient at the surface of nanoparticles, while the second slower exponential release is due to the diffusion of the active ingredient from the nanoparticles. The cyclic oligosaccharide release is very rapid.

When the active ingredient is soluble (such as in doxorubicine), the stabilizing role of the cyclic oligosaccharide is the most relevant. The active ingredient is present in the polymeric nucleus, while the oligosaccharide is at the surface of the nanoparticles.

In this case, only the second phase of release is observed for the active ingredient. The cyclic oligosaccharide release stays very rapid.

The prior art fails to teach or suggest this.

In light of the foregoing, we respectfully submit that the entire Application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,

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